acquiescence with regard to the Examiner's rejections, and are made without prejudice to prosecution of any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application. Corrected drawings are submitted herewith in reply to the Examiner's request.

Rejection Under 35 U.S.C. § 112, First Paragraph (enablement)

Claims 4-10, 16, 58 and 60 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification allegedly does not enable any person skilled in the art to make or use the invention commensurate in scope with the current claims. The Examiner acknowledges that the specification is enabling for an isolated polynucleotide comprising the sequence of SEQ ID NO: 107, polynucleotides encoding fusion proteins comprising SEQ ID NO: 107, as well as vectors and host cells comprising SEQ ID NO: 107. The Examiner further acknowledges that the polynucleotide of SEQ ID NO: 107 has a differential expression pattern in prostate cancer tissue relative to normal prostate tissue. Despite this disclosure, however, the Examiner takes the position that the specification does not reasonably provide enablement for portions or variants of SEQ ID NO: 107, apparently because the specification has allegedly not taught the activity or biological function common to the claimed the genus of polynucleotides. For example, the Examiner takes the position that :

> "With regard to variants of the polynucleotide of SEQ ID NO: 107, since the specification does not teach the function or biological activity of the polypeptide of SEQ ID NO; 108, nor an assay to measure such, the skilled artisan would not know which modifications to the polypeptide sequence of SEQ ID NO: 108 would result in a polypeptide with altered biological activity."

Applicants respectfully traverse this basis of rejection and submit that the specification does, in fact, provide enablement for the claimed invention. As set forth in the above amendment, newly added claims 64-72 are drawn to isolated polynucleotides comprising SEQ ID NO: 107, isolated polynucleotides comprising at least 75 or 150 consecutive residues of SEQ ID NO: 107, isolated polynucleotides having at least 75%, 85% or 95% identity to the entirety of SEQ ID NO: 107 and isolated polynucleotides having at least 90% identity to a sequence comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107.

Thus, in order to practice the claimed invention, the skilled artisan simply needs

to understand how to make and use fragments of SEQ ID NO: 107 and how to make and use sequences having some defined degree of structural identity to SEQ ID NO: 107. This subject matter is indeed fully enabled by Applicants' specification as originally filed, wherein extensive illustrative guidance regarding making and using fragments and variants of Applicants' cancer-associated sequence is offered (*e.g.*, page 36, line 20 to page 37, line 11; page 34, line 16 to page 36, line 19).

Applicants further submit the current claims are drawn to isolated polynucleotides, not isolated polypeptides, and that it is the prostate tumor-associated expression profile identified by Applicants for SEQ ID NO: 107, not the biological function of the encoded polypeptide of SEQ ID NO: 108, that is most pertinent to enablement of the presently claimed invention. The skilled artisan, for example, would appreciate that the biological function of SEQ ID NO: 108 is irrelevant to the over-expression of SEQ ID NO: 107 in prostate cancer tissue relative to normal tissue and, similarly, is irrelevant to how fragments and variants of SEQ ID NO: 107 can be made and used in a diagnostic context according to Applicants' disclosure.

As acknowledged by the Examiner, SEQ ID NO: 107 possesses a prostate cancer-associated expression profile sufficient to distinguish prostate cancer tissue from normal prostate tissue. In view of this disclosure, the individual skilled in the diagnostic arts would immediately appreciate that SEQ ID NO: 107 can be used, for example, as a diagnostic marker for prostate cancer. In one illustrative scenario, the species of SEQ ID NO: 107 can be used as a probe to detect expression of a mRNA corresponding to SEQ ID NO: 107 in a biological sample, using routine hybridization-based techniques. If a biological sample suspected of being cancerous is found to exhibit over-expression of SEQ ID NO: 107 relative to a suitable negative control using these art-recognized techniques, such a finding is indicative that the biological sample indeed contains cancerous prostate tissue, otherwise over-expression of SEQ ID NO: 107 would not have been detected.

Applicants submit that the skilled artisan would further appreciate, in view of this disclosure, that the genus encompassed by fragment and % identity language of the current claims is also fully enabled by the specification. More particularly, the skilled artisan, upon accepting that SEQ ID NO: 107 can be used in any of a number of hybridization-based assays for detecting expression of this sequence in a biological sample, would also understand that the claimed fragments and variants of SEQ ID NO: 107 can be used in the very same context and to

the same extent as the specific species of SEQ ID NO: 107, despite the fact that they are not identical to the species of SEQ ID NO: 107. For example, based upon fundamental principles of DNA and RNA hybridization properties, it would be understood that the claimed genus of fragments of SEQ ID NO: 107 can be made and used, without undue experimentation, to detect expression of SEQ ID NO: 107 in a biological sample, and are thus useful in the context of Applicants disclosure in the same manner as for the species of SEQ ID NO: 107. Moreover, it would be further understood that the claimed genus of variants of SEQ ID NO: 108, *e.g.*, sequences related by structural identity to SEQ ID NO: 107, can be made and used, without any undue experimentation, to similarly detect expression of SEQ ID NO: 107, irrespective of whether they are identical to the species of SEQ ID NO: 107. The skilled artisan, rather, would understand and appreciate that the claimed genus of polynucleotides would be capable of specifically hybridizing to the species of SEQ ID NO: 107, and, consequently, would be useful in detecting expression of SEQ ID NO: 107 in a biological sample. As the individual skilled in the diagnostic arts would understand and concur that such fragments and variants of SEQ ID NO: 107 can be readily and routinely made and used in the context of Applicants' disclosure, they are submitted to fall squarely within the scope of enabled subject matter.

Reconsideration and withdrawal of the Examiner's rejection under 35 U.S.C. §112, first paragraph, is thus respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph (written description)

Claims 2 and 7 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicants, at the time the application was filed, had possession of the claimed invention. The Examiner acknowledges that Applicants are in possession of SEQ ID NO: 107 and that this polynucleotide has a prostate cancer-associated expression pattern. However the Examiner asserts that the specification has not described a biological function or activity for the encoded polypeptide of SEQ ID NO: 108 and concludes on this basis that Applicants were not in possession of any sequence other than the polynucleotide species of SEQ ID NO: 107.

As noted above, newly added claims 64-72 are drawn to isolated polynucleotides comprising SEQ ID NO: 107, isolated polynucleotides comprising at least 75 or 150 consecutive

residues of SEQ ID NO: 107, isolated polynucleotides having at least 75%, 85% or 95% identity to the entirety of SEQ ID NO: 107 and isolated polynucleotides having at least 90% identity to a sequence comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107.

Applicants respectfully traverse the Examiner's rejection and submit that the specification more than adequately describes relevant and distinguishing identifying characteristics sufficient to establish that Applicants were in possession of the genus of polynucleotide currently claimed at the time the application was filed. Applicants further submit that biological function is but one example of an identifying characteristic sufficient to support a claimed genus of polynucleotides and/or polypeptides. Under the Examination Guidelines set forth by the Patent and Trademark Office, the written description requirement for a claimed genus may be satisfied by the description of a representative number of species or the disclosure of relevant, identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099, at 1106 (emphasis added).

Applicants submit that an illustrative sufficient and relevant identifying characteristic shared by members of the currently claimed genus is their ability to be used in the detection of prostate cancer. As noted above, the biological function of the polypeptide of SEQ ID NO: 108 is not relevant to the over-expression of SEQ ID NO: 107 in cancer tissue relative to normal tissue or to its ability to be used in the detection of prostate cancer according to Applicants' disclosure, and would be recognized as such by the skilled individual. Accordingly, Applicants submit that the prostate tumor-associated expression profile of SEQ ID NO: 107 represents an identifying characteristic, described in the specification as filed, sufficient to convey to the artisan skilled in the diagnostic arts that applicants were in possession of the claimed genus of polynucleotides.

Given Applicants' disclosure of the novel P504S polynucleotide of SEQ ID NO: 107, in conjunction with Applicants' discovery that this polynucleotide is over-expressed in prostate cancer tissue relative to normal tissues, the skilled artisan would further recognize that Applicants were in possession of much more than the specific sequence of SEQ ID NO: 107. In view of this disclosure, and further in view of the level of general knowledge in this art, the skilled artisan would understand and expect that a genus of polynucleotides structurally related to SEQ ID NO: 107, *e.g.*, sequences having at least 75%, 85% or 95% identity to SEQ ID NO: 107,

would also be useful in the context of Applicants' invention, in the same manner as for the specific sequence of SEQ ID NO: 107. For example, the skilled artisan would appreciate that such sequences related to SEQ ID NO: 107 can be used, for example, in detecting expression of SEQ ID NO: 107 in a biological sample, and are thus useful in the detection of prostate cancer, despite the fact that the sequences are not identical with the specific sequence of SEQ ID NO: 107. This understanding and expectation on the part of the skilled artisan is submitted to be soundly based upon fundamental scientific principles, namely that a polynucleotide having at least 75%, 85% or 95% identity to SEQ ID NO: 107, although structurally distinct from SEQ ID NO: 107, can nonetheless specifically hybridize to SEQ ID NO: 107 and can thus be used to detect expression in a biological sample of a sequence comprising SEQ ID NO: 107. Accordingly, to accept the Examiner's position that Applicants were only in possession of the specific species of SEQ ID NO: 107 would improperly exclude an entire class of isolated polynucleotides that the skilled individual would understand were clearly in Applicants' possession at the time of filing. Reconsideration of the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 4-7 and 58-59 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. More specifically, the Examiner views as indefinite Applicants' use of the phrases "recited in", "substantially diminished", "the protein", and "complementary".

As set forth in the above amendment, claims 1-63 have been cancelled and newly added claims 64-72 are drawn to isolated polynucleotides comprising SEQ ID NO: 107, isolated polynucleotides comprising at least 75 or 150 consecutive residues of SEQ ID NO: 107, isolated polynucleotides having at least 75%, 85% or 95% identity to the entirety of SEQ ID NO: 107 and isolated polynucleotides having at least 90% identity to a sequence comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107.

Applicants respectfully submit that the allegedly indefinite phrases noted by the Examiner have been removed from new claims 64-72, without prejudice or acquiescence. Applicants further submit that new claims 64-72, in accordance with 35 U.S.C. § 112, second

paragraph, are clear and unambiguous in conveying to the skilled artisan the metes and bounds of Applicants' invention. Reconsideration and withdrawal of the Examiner's rejection is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 5 and 6 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Accession number U89906. According to the Examiner, U89906 teaches a polynucleotide having 48.8% identity to SEQ ID NO: 107. On this basis, the Examiner asserts that the cited sequence discloses a "variant" of SEQ ID NO: 107.

Claim 59 also stands rejected under 35 U.S.C. § 102(a) over accession number A48221, on the basis that this reference teaches an oligonucleotide comprising 10-40 nucleotides "recited in" SEQ ID NO: 107. According to the Examiner, the cited sequence teaches that nucleotides 111-159 of A48221 are identical to nucleotides 1573-1621 of SEQ ID NO: 107.

Claims 4 and 6-8 also stand rejected under 35 U.S.C. § 102(b) over Brennan (U.S. Patent No. 5,474,796), on the basis that this reference teaches an array of trimers including the trimer AAA which is asserted to be a complement of SEQ ID NO: 107.

Claims 7 and 58 also stand rejected under 35 U.S.C. § 102(b) over accession number G21632, on the basis that this sequence teaches a fragment of SEQ ID NO: 107 that is "almost identical" to the complement of SEQ ID NO: 107 from positions 1395-1533.

Applicants respectfully traverse these rejections and request reconsideration in view of the above amendment. As set forth above, claims 1-63 have been cancelled and newly added claims 64-72 are drawn to isolated polynucleotides comprising SEQ ID NO: 107, isolated polynucleotides comprising at least 75 or 150 consecutive residues of SEQ ID NO: 107, isolated polynucleotides having at least 75%, 85% or 95% identity to the entirety of SEQ ID NO: 107 and isolated polynucleotides having at least 90% identity to a sequence comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107, and complete complements of the foregoing polynucleotides. This currently claimed subject matter is submitted to be clearly novel over the references cited by the Examiner as the sequences corresponding to these accession numbers simply do not teach each and every element of any isolated polynucleotide encompassed by claims 64-72. More specifically, the cited references fail to disclose any sequence comprising at least 75 or 150 consecutive residues of SEQ ID NO: 107, fail to disclose any sequence having at

least 75%, 85%, or 95% identity to the entire full length of SEQ ID NO: 107, and similarly fail to disclose any sequence having at least 90% or 95% identity to a sequence comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107. Accordingly, new claims 64-72 are novel over the cited references. Reconsideration and withdrawal of the Examiner's rejections under 35 U.S.C. § 102 is thus respectfully requested.

Provisional Double Patenting Rejection

Claims 4-6, 9-10 and 59 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 6,262,245. According to the Examiner, claim 1 of the '245 patent is drawn to an isolated DNA molecule comprising the sequence of SEQ ID NO: 107, and is thus co-extensive in scope with certain currently pending claims in the instant application. Applicants acknowledge this rejection and respectfully submit that a Terminal Disclaimer will be filed in due course to the extent appropriate in view of subject matter deemed allowable by the Examiner in the instant application.

Claims 4-10 and 59 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-4 of copending applications serial nos. 09/895,814, 09/780,669, and 09/759,143. The Examiner notes that this is a provisional obviousness-type double patenting rejection because the potentially conflicting claims have not been patented. Applicants acknowledge this provisional rejection and respectfully submit that this issue will be addressed in due course, upon identification of allowable subject matter in the instant application.

Claims 4-10, 16 and 58-60 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-10, 16 and 58-60 of copending application serial nos. 09/636,215, 09/593,793, 09/605,783 and 09/568,100. The Examiner notes that this is a provisional obviousness-type double patenting rejection because the potentially conflicting claims have not been patented. Applicants acknowledge this provisional rejection and respectfully submit that this issue will be addressed in due course, upon identification of allowable subject matter in the instant application.

Attached hereto is a marked-up version of the changes made to the claims by the

current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

Favorable reconsideration and allowance of the currently pending claims are respectfully solicited. The Examiner is invited to contact the undersigned at 206-694-4885 with any questions, comments and/or suggestions pertaining to this communication.

Respectfully submitted,

Jiangchun Xu et al.

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please add new claims 64-72, as follows:

64. (New) An isolated polynucleotide comprising SEQ ID NO: 107.

65. (New) An isolated polynucleotide comprising SEQ ID NO: 107, or a fragment thereof comprising at least 75 consecutive nucleotide residues of SEQ ID NO: 107.

66. (New) An isolated polynucleotide comprising SEQ ID NO: 107, or a fragment thereof comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107.

67. (New) An isolated polynucleotide comprising a sequence having at least 75% identity to the entirety of SEQ ID NO: 108.

68. (New) An isolated polynucleotide comprising a sequence having at least 85% identity to the entirety of SEQ ID NO: 107.

69. (New) An isolated polynucleotide comprising a sequence having at least 95% identity to the entirety of SEQ ID NO: 107.

70. (New)An isolated polynucleotide having at least 90% identity to a sequence comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107.

71. (New) An isolated polynucleotide having at least 95% identity to a sequence comprising at least 150 consecutive nucleotide residues of SEQ ID NO: 107.

72. (New) An isolated polynucleotide comprising a complete complement of a polynucleotide according to any one of claims 64-71.